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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,291	YONEHARA ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, and 4-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on December 27, 2007, has been received and entered.

Claim 3 is canceled.

Claims 1, 2, 4-30 are pending in this application and were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/27/2007 has been entered.

Double Patenting Rejections

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or

would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of Yonehara et al. US Patent No. 6,790,665. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 1-22 of Yonehara et al. recite a method comprising: determining an amount of total hemoglobin in a sample containing glycated hemoglobin by causing a reaction between a glycation site of the denatured hemoglobin and a fructosyl amino acid oxidase, measuring the degree to which the redox reaction has occurred to determine an amount of the glycated hemoglobin, and calculating a ratio of the glycated

hemoglobin to the total hemoglobin in the sample from the amount of the total hemoglobin and the amount of the glycated hemoglobin, wherein the denatured hemoglobin is treated with a protease, the hemoglobin in the sample is treated with the tetrazolium compound in the presence of a surfactant, the tetrazolium compound is 2-(4-iodophenyl)-3- (2,4-dinitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium salt, a method wherein the color-developing substance is a substrate that develops color by oxidation and has developed color as a result of a reaction caused by an oxidase between the hydrogen peroxide and the substrate.

Applicant's arguments filed on 12/27/2007 have been fully considered but they are not persuasive.

Applicant argues that Yonehara et al. fail to recite the steps of causing a fructosyl amino acid oxidase to act on a glycated amino acid present in the sample so that the analyte remains in the sample and the glycated amino acid is removed from the sample, so that the analyte remains in the sample and then measuring the amount of the analyte. Applicant argues that Yonehara et al. fail to recite or suggest a measuring kit.

However, Yonehara et al. recite a method comprising a reaction between a glycation site of the denatured hemoglobin obtained and a fructosyl amino acid oxidase (see column 21 claim 12). Yonehara et al. also recite degrading hemoglobin with a protease (column 22 claim 15).

Please note that, in the initial step of the Maillard reaction glucose is attached to the α or ε amino group of amino acids and proteins to form unstable Schiff's base and become rearranged to form glycation products. Thus, the glycation site taught in Yonehara et al. is the glycated amino acid(s) in the sample.

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the claimed method disclosed by Yonehara et al. to measure an amount of glycated protein in a sample using a redox reaction. Furthermore, once an enzymatic determination of a glycated protein was established, providing a measuring kit to determine the amount of the glycated protein would become obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn due to applicant amendments to the claims filed on 12/27/2007.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 4-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Komori et al. (European patent application, EP1 002874 A2, Published June 24th, 2000) in view Montellano et al. (Biochemistry, 1988, Vol. 27, pp. 5470-5476) and further in view of Ishimaru et al. (Patent number 6,127,138, Date of Patent Oct. 3, 2000), and further in view of Kwan et al. (Us patent No. 5,556,788).

Claims 1, 2, and 4-30 are drawn to a method of measuring an amount of a glycated protein as an analyte in a sample, comprising: causing a fructosyl amino acid oxidase (FAOD) to act on a glycated amino acid present in the sample so that the analyte remains in the sample and the glycated amino acid is removed form the sample by degradation; degrading the analyte with a protease to give a degradation product of the analyte either before or after causing the fructosyl amino acid oxidase to act on the glycated amino acid; then causing a fructosyl amino acid oxidase to act on a proteolytic degradation product of the analyte to cause a redox reaction in the presence of a tetrazolium compound and sodium azide; and measuring an amount of hydrogen peroxide generated by the redox reaction to determine the amount of the analyte, wherein the measurement of the amount of hydrogen peroxide comprises adding a color-developing substrate to allow a redox reaction between the color-developing substrate and the hydrogen peroxide, and measuring an amount of color developed by the color-developing substrate to determine the amount of hydrogen peroxide further comprises, adding N- (carboxymethylaminocarbonyl)-4,4'-bis(dimethylamino) diphenylamine sodium salt as a color-developing substrate to a reaction solution of the redox reaction in the presence of a surfactant, a concentration of the tetrazolium compound in the reaction solution is in a range from 0.5 to 8 mmol/1, a concentration of

the sodium azide in the reaction solution is in a range from 0.08 to 0.8 mmol/1, a concentration of the surfactant in the reaction solution is in a range from 0.3 to 10 mmol/1, and a pH of the reaction solution is in a range from 7.0 to 8.5, the tetrazolium compound is 2-(4-iodophenyl)-3-(2,4-dinitrophenyl)-5- (2,4-disulfophenyl)-2H-tetrazolium salt, and a measuring kit for measuring a glycated protein.

Komori et al. teach a method of measuring an amount of a glycated protein as an analyte in a sample, comprising: causing a fructosyl amino acid oxidase (FAOD) to act on a glycated amino acid present in the sample so that the analyte remains in the sample and the glycated amino acid is removed form the sample by degradation; degrading the analyte with a protease to give a degradation product of the analyte either before or after causing the fructosyl amino acid oxidase to act on the glycated amino acid; then causing a fructosyl amino acid oxidase to act on a proteolytic degradation product of the analyte to cause a redox reaction in the presence of a tetrazolium compound and sodium azide; and measuring an amount of hydrogen peroxide generated by the redox reaction to determine the amount of the analyte, wherein the measurement of the amount of hydrogen peroxide comprises adding a color-developing substrate to allow a redox reaction between the color-developing substrate and the hydrogen peroxide (page 2, 0002-0004, and page 4 0029 and 0030).

Komori et al. teach adding a tetrazolium compound prior to the redox reaction or pretreating a sample with a tetrazolium compound to eliminate the influence of any reducing substance (Page 2 0010, and page 8 0072), and further teach the formation of hydrogen peroxide due to the oxidation of glycated proteins by the action of FAOD enzyme, and further teach both glycated peptides (proteins) and glycated amino acids

can be subjected to the action of FAOD and glycated proteins and peptides are treated with a protease before its treatment with FAOD (Page 4, Lines 7-9).

Komori et al. teach the color developing substrate N-(carboxymethylaminocarbonyl)-4,4'-bis(dimethylamino) diphenylamine sodium salt (DA-64) as (Page 4, Lines 3-5) and teach adding a surfactant so that its concentration in the treating solution falls in the range of 0.01- 5% by weight (Page.6 Line 5) and the concentration of tetrazolium compound (WST-3) is 1 mmol/L (Page 8, Lines 26 and 27).

Komori et al. teach a peroxidase (POD) having a concentration equal to 219 KU/L (Page 17, 0095) and a reducing agent are added to the sample (Page 2, Line 12). Sigma-Aldrich catalogue discloses an active form of metalloproteinase in 10mM MES buffer, containing 0.25 mM sodium chloride and 5 mM calcium chloride and 0.01% sodium azide.

Komori et al teach non-ionic surfactants such as Triton X-100 series, Tween series, Brij series and the like (page 5-6, 0044). The pretreatment is usually carried in a buffer and further recites CHES, CAPSO, CAPS, phosphate, Tris, EPPS, HEPES, pH range 8-12 (Page 6, 0047).

Komori et al. teach FAOD treatment is carried out in the protease treatment solution for which a Tris-HCl, EPPS, or PIPES buffer can be used and the concentration of FAOD in the reaction solution is 50-50,000 U/L and pH of 6-9 (Page 6, 0052,0055) and 0.146 mM DA-64 (Page 17, 0095). Komori et al. also recites uricase (page7, 0066) and bilirubin oxidase (Page 7, 0064).

Applicant's arguments filed on 12/27/2007 have been fully considered but they are not persuasive.

Applicant argues that nothing in Komori teaches or suggests the method of measuring the amount of glycated protein as the analyte involving the steps of causing a FAOD to act on a glycated amino acid present in the sample so that the analyte remains in the sample and the glycated amino acid is removed from the sample, and then measuring the amount of the analyte as required by claim1.

Applicant argues that the FAOD treatment step of Komori does not correspond to the step of causing a FAOD to act on a glycated amino acid present in the sample, so that the analyte remains in the sample and the glycated amino acid is removed from the sample as required by claim 1.

However, Komori et al. teach the analyte is glycated amino acid and the glycated amino acids are subject to the action of FAOD (page 4 0029-0030). Moreover, amended claim 1 recites "…causing a FAOD to act on a glycated amino acid …. that the analyte remains in the sample and the glycated amino acid is removed from the sample by degradation". The broadest reasonable interpretation of "so that the analyte remains in the sample and the glycated amino acid is removed from the sample by degradation" would be that the glycated amino acid is removed by the degrading action of the enzyme FAOD – this is the claim construction the examiner has used to examine the claims.

Komori et al. do not teach a measuring kit, aging a solution containing tetrazolium compound and sodium azide. However, Kwan et al. teach storing a reagent comprising tetrazolium compound by leaving the solution to stand at temperature in the

range of 20-60ºC for 6 to 120 hours (column 4 lines 46-48), and further teach, adding sodium azide to a control reagent and incubating for 4 days at 37ºC(column 6 lines 37-50). Also, Montellano et al. teach azide anion functions as an inhibitor of catalytic hemoproteins like catalase and horseradish peroxidase and using 0.15-0.6 mM sodium azide (Pg 5470 Introduction, Pg 5471, 3rd Paragraph).

Further motivation is in Ishimaru et al. who teach a method of measuring glycated protein in a sample by causing an oxidoreductase (an enzyme that catalyzes an oxidation-reduction or redox reaction) to act on glycated protein and measuring the amount of the product based on the action of the enzyme (Col.1, lines 61-66). Also, Ishimaru et al. teach measuring a glycated protein for the purpose of the diagnosis of diabetes and further teach the method is applicable to a general-purpose examining apparatus with lower cost for a shorter period of time (Col. 2, Lines 41-44).

Applicant argues that the rejection's analysis of Komori has been tainted by the improper use of hindsight, that the FAOD treatment of Komori does not involve removing unwanted glycated amino acid from the sample such that the glycated amino acid itself is not measured.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Therefore, it would have been obvious to one of the ordinary skill in the art, to add sodium azide as taught by Kwan et al. and Montellano et al. to the reagent in the method of measuring glycated hemoglobin as taught by Komori, and to provide a method of measuring an amount of a glycated protein as an analyte in a sample. The motivation as taught by Montellano et al. would be, that sodium azide was able to inhibit the breakdown of hydrogen peroxide by the catalase released into the sample as a result of hemolzying erythrocytes and thus interfere with the measurement, also to prevent bacterial contamination.

Moreover, it would have been obvious to provide a kit for measuring a glycated protein using a redox reaction using the method as taught by Komori et al. The motivation as taught by Ishimaru et al. would be to provide an examining apparatus with lower cost and in a shorter period of time for the purpose of the diagnosis of diabetes.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Kade Ariani
Examiner
Art Unit 1651